REMARKS

Claims 56-68 were previously pending, are amended herein, and are presented for reconsideration. No new matter has been added by virtue of the amendments to the claims.

In accordance with the Examiner's suggestion, the claims have been amended to substitute the word "composition" for the word "agent" and to add a comma before the word "wherein." These amendments do not result in any change in claim scope.

The amendment of claim 56 is supported by the specification at page 9, lines 1-45, which identifies examples of subjects, including humans, in need of treatment by the claimed invention; at page 1, lines 17-19, which teaches local administration of a therapeutic in accordance with the present invention; and at page 10, lines 12 and page 16, lines 13-15, which teach increasing the diameter of a biological conduit (e.g. an artery or vein).

Certain claims have been amended to eliminate dependence on a non-preceding claim. Claim 58, as amended, corresponds with claim 61 as previously pending. Claim 59, as amended, corresponds with claim 58 as previously pending. Claim 61, as amended, corresponds with claim 59 as previously pending. These amendments do not result in any change in claim scope.

Claim 67 has been amended, in accordance with the Examiner's suggestion, to clarify that the term "isolated" does not refer to explantation from the body of the human subject.

I. Objections to Supplemental Information Disclosure Statement

The Supplemental Information Disclosure Statement, filed on December 15, 2003, citing references AA-AY, has been objected to on the ground that it lacks the fee required under 37 C.F.R. § 1.17(p). Office Action at 2.

In connection with the presently filed RCE, Applicants are also filing an accompanying Information Disclosure Statement (IDS) citing the same references AA-AY, thereby obviating this objection. Copies of references AA-AY were previously submitted in connection with this application. Copies of additional references AZ and BA are submitted herewith.

II. Objections to Claims

Claims 59-60 were objected to as dependent from a non-preceding claim. These claims, as amended, no longer depend from a non-preceding claim, thereby obviating this objection.

III. Rejections Under 35 U.S.C. § 112.

Claim 56 and its dependent claims were rejected under 35 U.S.C. § 112, second paragraph, as indefinite on the ground that recitation of the phrase "susceptible to obstruction" was vague, unclear and confusing. Claim 56, as amended, no longer recites the phrase in question, thereby obviating the rejection.

Claim 66 is directed to a method of treating an artery or vein that is susceptible to obstruction by a particular type of lesion called "intimal hyperplasia." The specification explains what intimal hyperplasia is (*see* Specification at page 4, lines 16-23) and identifies vessels that are at risk of obstruction from this lesion. *See id*, at page 4, line 14 to page 5, line 3 and page 16, line 26 to page 17, line 11. In this regard, applicant respectfully points out that the claimed method need not prevent intimal hyperplasia from occurring in order to benefit the artery or vein being treated. On the contrary, the method as presently claimed reduces the likelihood or the extent of obstruction, even if intimal hyperplasia occurs, by increasing the diameter of the treated artery or vein itself, not merely the diameter of the lumen. A larger diameter artery or vein is better able to tolerate intimal hyperplasia without becoming obstructed. *See* Specification at page 16, lines 13-15 (teaching that "the increased conduit diameter obviates the potential of obstruction formation within a conduit."). Thus, the method as claimed ameliorates the deleterious consequences of intimal hyperplasia, without necessarily preventing intimal hyperplasia from occurring.

Claims 56-59, 61, 67-68 and their dependent claims were rejected under 35 U.S.C. § 112, second paragraph, as indefinite on the ground that recitation of the phrase "an agent comprising" was vague, unclear and confusing. In accordance with the Examiner's suggestion, the claims have been amended to recite "a composition comprising," thereby obviating this rejection.

IV. Rejections Under 35 U.S.C. § 102.

Claims 56-57 were rejected under 35 U.S.C. § 102(b) as anticipated by Anidjar *et al.*, Annals of Vascular Surgery 8: 1128-1136 (1994) ("Anidjar"). Applicant respectfully points out that Anidjar concerned administration of pancreatic elastase to a rat aorta in order to produce an experimental aneurysm. Anidjar does not teach or suggest administering elastase to an artery or vein in a human subject, as required by claim 56. Nor does Anidjar teach or suggest administering elastase to a subject (whether human or not) that is in need of such treatment, as required by the presently amended claims. Prior art use of elastase to produce pathological lesions of vessels for purposes of medical experiments -- to the detriment of the experimental animals used in those studies -- does not teach or suggest the presently claimed method, in which elastase or collagenase is administered to benefit a human subject in need of such treatment. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

Claims 56-57 were rejected under 35 U.S.C. § 102(b) as anticipated by Ooyama *et al.*, The Molecular Biology and Pathology of Elastic Tissues (Ciba Foundation Symposium 192) pp. 307-320 (1995) ("Ooyama"). The teachings of Ooyama concern oral administration of porcine pancreatic elastase I (PPEI) to elderly patients in order to reduce the age-related increase in blood cholesterol, pulse wave velocity, and intimal thickening of the carotid artery. *See* Ooyama at 312. Ooyama describes the administration of purified PPE1 in a daily oral dose. The systemic administration taught by Ooyama stands in contrast with local administration of elastase or collagenase in the vicinity of the wall of an artery or vein, as required by the presently amended claims, *e.g.*, by delivering the recited composition adjacent to, onto, or into the wall of the artery or vein at or near a site to be treated.

Nor does Ooyama disclose administering to a human subject (whether locally or systemically) elastase in such a manner as to cause proteolysis of elastin in the wall of the artery or vein, as required by claim 56 and its dependent claims. On the contrary, the discussion section of the Ooyama reference reveals that although the authors could detect immunoreactive fragments of PPEI in the blood, as measured by ELISA, after oral administration (*see id.* at 313), they were unable to demonstrate the presence of enzymatically active PPEI in the circulation. *See id.* at 318 (conceding that the authors were "unable to demonstrate an increase of elastolytic activity"). In fact, the discussion in Ooyama suggests that "the beneficial effect of the treatment must stem from a property of the protein separate from its enzymatic activity." *Id.* at 319. Indeed, Ooyama teaches that "fragmentation [of elastin] is prevented by the simultaneous administration of PPE1." *Id* at

315. Accordingly, Ooyama fails to teach administration of elastase in a manner that results in proteolysis of elastin in the vessel wall, as required by the claims.

Furthermore, Ooyama fails to teach administering elastase (whether locally or systemically) in such a manner as to cause enlargement of the diameter of the artery or vein, as required by claim 56 and its dependent claims, for the following two reasons.

First, applicant respectfully points out that Ooyama does not teach "administering a composition comprising elastase to reduce thickness of artery wall," as stated in the Office Action at page 4 (citing Ooyama at 314-315). Rather, Ooyama teaches prophylactic oral administration of elastin to modulate "the age-related increase in . . . the intimal-medial thickness of the carotid artery". Ooyama at 314; see also *id.* at 315 (teaching that long-term oral administration of PPEI to elderly patients modulates "the age-related increases in PWV and intimal thickening of the carotid artery."). In other words, the method of Ooyama does not cause the arterial wall to become thinner, but rather moderates the extent to which the walls of arteries become thicker as part of the ageing process. Even this latter teaching is not supported in Ooyama by any data, but only by reference to a "personal communication" from a third party. *See* Ooyama, page 314, lines 12-14 underneath Figure 6.

Second, even if Ooyama had taught reduction in the thickness of the artery wall, that still would not provide enlargement of the diameter of the artery or vein, as required by the presently amended claims. Reducing the thickness of the vessel wall might enlarge the lumen of the vessel, but would not enlarge the diameter of the vessel itself.

For each of the above reasons, Applicant submits that the rejection over Ooyama should be withdrawn.

V. Rejections Under 35 U.S.C. § 103(a).

Claims 56-68 were rejected under 35 U.S.C. § 103(a) as obvious over Anidjar and Ooyama in view of Strindberg *et al.*, Journal of Investigative Surgery 11: 185-198 (1998) ("Strindberg").

The deficiencies of the primary references, Anidjar and Ooyama, are discussed above. These deficiencies are not remedied by the secondary reference, Strindberg, which is concerned with administering elastase, alone or in combination with collagenase, to the aorta of dogs so as to cause experimental aneurysms. Because Strindberg teaches methods that result in aortic aneurysm – which is highly undesirable in humans – it teaches away from the presently claimed method, which is directed to treating an artery or vein in a human subject.

No human subject could properly be regarded as being in need of treatment according to the method of Strindberg.

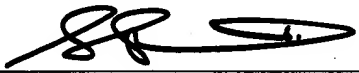
Accordingly, Applicant respectfully requests that the rejection under § 103(a) be withdrawn.

CONCLUSION

In the light of the above amendments and remarks, the Applicant respectfully requests that the Examiner enter this Amendment and allow the claims as herein amended. The Examiner is invited to call the undersigned attorney at (212) 859-8973 if a telephone call could help resolve any remaining issues.

Respectfully submitted,

Date: September 27, 2004



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